UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,669	11/08/2005	Hesson Chung	4698-0109PUS1	9231

2292 7590 12/11/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
PALENIK, JEFFREY T	
ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
12/11/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/521,669	CHUNG ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,10-13,16,27-33,37,38,42,43,48-51,54 and 65-78* is/are pending in the application.

4a) Of the above claim(s) *16,28-33,37,38,42,43,48-51,54,65-71 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,10-13,27,72,73 and 75-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

STATUS OF THE APPLICATION

Receipt is acknowledged of Applicants' Amendments and Remarks filed, filed 17 August 2009, in the matter of Application N° 10/521,669, in response to the Notice of Non-Responsiveness mailed by the Office on 17 June 2009. Said filings are entered on the record. The Examiner further acknowledges the following:

Claims 75-77 were added previously, with support in the original claims (e.g. claims 1 and 72), but were inadvertently overlooked by the Examiner.

Claim 78 is newly added and garners support from the originally presented base claim.

No claims are newly cancelled.

Claims 1, 5, 6, 10-13, 27, 72 and 73 have all been amended for clarity with support being lent from the original submission. Claim 1 has been further amended to reflect narrower weight percent ranges for the recited components.

No new matter has been added.

Thus, claims 1, 5, 6, 10-13, 27, 72, 73 and 75-78 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been filed for consideration.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicants' amendment which sets forth the Abstract to the Invention on a separate page is sufficient to render moot the objection.

Rejections under 35 USC 112

Applicants' amendments to claims 1, 5, 10 and 73 are sufficient enough to render moot the indefiniteness rejection under 35 USC 112, second paragraph. Thus, said rejection has been **withdrawn**.

Rejections under Double Patenting

Applicants' remarks concerning the rejection of claims 1, 5, 6, 10-13, 27, 72 and 73 on the grounds of provisional non-statutory obviousness-type double patenting are considered unpersuasive by the Examiner. However, the copending '989 Application contains a terminal disclaimer which was filed on 17 August 2009 and approved on 20 August 2009. Said terminal disclaimer has been recorded as being filed to distinguish itself from the instant application. As such, the rejection of provisional non-statutory obviousness-type double patenting stands **withdrawn**.

US Application N° 10/521,695 has been abandoned thereby rendering moot the rejection under provisional non-statutory obviousness-type double patenting.

MAINTAINED REJECTIONS

The following rejection is maintained from the previous Office Correspondence dated 28 October 2008 since either the grounds or art on which they were previously set forth continues to read on the amended limitations.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 6, 10-13, 27, 72, 73 and 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al. (USPN 6,521,139).

The instant claims are directed to a mucoadhesive formulation comprising, by weight, 4-90% of at least one monoolein compound, 0.01-90% of an oil and 0.01-20% of paclitaxel, wherein the ratio of monoolein to oil is greater than 1:1 (claim 1). Claim 73 further limits the composition of claim 1 such that it narrows the percent ranges of each of the claimed components. Additional limitations to the oil component are recited in claims 5 and 6. The composition is recited as further comprising 0.01-5% of an additive such as the elected paclitaxel derivatives, which are insoluble, anticancer drugs (claims 10-13). The administration route limitation in claim 27 is considered by the Examiner to be a recitation of intended use, since said limitation does not serve to further limit the actual composition. Claim 72 recites that the formulation be either liquid or semi-solid.

Gao et al. teach a pharmaceutical composition comprising a pharmaceutically active agent, a glyceride mixture consisting essentially of diglyceride and monoglyceride, one or more pharmaceutically acceptable solvents and one or more pharmaceutically acceptable surfactants (claim 1). The glyceride ratio is further taught in claim 1 as ranging from about 9:1 to about 6:4 by weight. Claims 8 and 10 respectively teach that the monoglyceride is monoolein and that the di-/monoglyceride compound exists in the composition in an amount between about 5% to about 40% by weight. Given that the monoglyceride portion of the glyceride component is taught as ranging from about 10-40% and that the overall glyceride component ranges compositionally

from about 5-40% by weight, it follows that said monoglyceride is taught as being in the composition ranging overall from about 0.5% to about 16% by weight. Triacetin, which is a triglyceride compound whose branches each have 2 carbon atoms, is taught as a surfactant in claim 1. Claim 19 further teaches the surfactant as being present in the composition between about 10-50% by weight. Claims 2 and 5 teach paclitaxel and its derivative, docetaxel, as active agents and that said active is present in the composition between about 5-30% by weight, respectively. The composition is further and preferably taught as taking the form of a liquid for the purposes of preparing soft elastic gelatin capsules for oral administration (col. 9, line 66 to col. 10, line 4).

Gao et al. do not expressly teach: (1) the ratio of monoolein to oil as being greater than 1:1, (2) paclitaxel derivatives as additives or in combination with paclitaxel, (3) the claimed additive percent range, or (4) the narrower claimed compositional percent ranges of claim 73.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising at least one monoolein, an oil, paclitaxel, and an additional additive in the form of a paclitaxel derivative, as suggested by Gao, modify the amounts and/or ratios of the ingredients, and produce the instant invention in a liquid format for use in an orally administered form.

One of ordinary skill in the art would have been motivated to do this because Gao expressly teaches a preparing a composition wherein the active agent is paclitaxel or one of its derivatives, such as docetaxel, in addition to the other aforementioned components. Preparation of the composition as a liquid for downstream use in a soft gelatin capsule format is also

preferred. Regarding the additive, though it is not expressly taught that the paclitaxel derivative docetaxel is used in combination with paclitaxel as an "additive", it would have been *prima facie* obvious to combine the two compounds within the same dosage form as both are taught in the art (e.g. claim 2) and as being used for the same purpose. The idea of combining the two compounds flows logically from their having been individually taught by Gao et al. (see MPEP §2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

Furthermore, while the reference does not expressly teach all of the percent ranges (e.g. claim 10 and 73) or the greater than 1:1 ratio of monoolein to oil, as claimed by Applicants, the values and formats of each parameter with respect to the claimed composition are adjustable. It thus follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. In the instant case, it would have been within the purview of the skilled artisan to adjust the amounts of both the monoolein and/or triacetin (oil triglyceride) compounds used in the composition in order to achieve a ratio of the two equating to greater than 1:1 (see MPEP §2144.05(II)(B.)). Similarly, it would have been customary for an artisan of ordinary skill, to further narrow the claimed compositional percentages, in order to achieve the desired formulation for solubilizing paclitaxel. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection of claims 1, 5, 6, 10-13, 27, 72 and 73 under 35 USC 103(a) as being unpatentable over the teachings of Gao et al. have been fully considered but they are not persuasive.

Applicants allege that the instantly claimed composition is not rendered obvious for the following reasons: first, that the composition taught by the Gao reference comprises diglycerides as a main component, whereas the instantly claimed composition does not. Applicants further state that diglycerides are not a part of the invention "because diglyceride compounds are very cytotoxic". Secondly, Applicants assert that the ratio of oil to monoolein taught by the Gao reference does not read on that which is instantly claimed. To support this statement, Applicants state, for example, that the instantly claimed oil:monoolein ratio ***cannot exceed*** 1.5:1 (e.g. 60 wt% oil to 40 wt% monoolein), while the minimum ratio of monoolein:oil (e.g. the reverse of the first ratio) in the claimed composition is more than 1:15 (e.g. 40 wt% monoolein to 60 wt% oil). Applicants then compare this to the ratios of monoglyceride to diglyceride (oil) taught by Gao. The ratio is taught as ranging from 9:1 to 6:4 monoglyceride:diglyceride (e.g. oil). Lastly, Applicants allege that the composition of the present application is clearly distinguishable from Gao in that the claimed composition "does not comprise an additional solubilizing agent such as Cremophor as a major component". Applicants further attest that the present invention "does not require" and "does not utilize" such surfactants as Cremophor since "[i]t is very well known to

one skilled in the art that the solubilizing agent Cremophor causes severe toxic side effects" and that "Cremophor EL may prevent efficient uptake of paclitaxel".

In response to the first allegation, the Examiner respectfully submits that Applicants' rejected composition, namely claim 1 is directed to a composition which "comprises" the drug, oil, and monoolein. That the composition "comprises" these components, does not preclude it from comprising any other components, such as diglycerides. Furthermore, Applicants' remarks concerning the cytotoxicity of diglycerides is unpersuasive considering that said compounds are very well known in the art as being Generally Recognized as Safe (GRAS).

Regarding Applicants' second argument, the Examiner respectfully disagrees and maintains that the Gao reference continues to read on the amended limitations since a monoglyceride:diglyceride ratio of 6:4 as taught by Gao is the equivalent of a 1.5:1 ratio. Furthermore, Applicants remarks concerning the claimed ratios of monoolein to oil and oil to monoolein appear to be seemingly contradictory. On the one hand, Applicants attest that the monoolein to oil cannot exceed 1.5:1, but that the oil to monoolein ratio exceeds 1:1.5 (e.g. 0.67:1). Respectfully, the ratios are considered by the Examiner as being the same, only reversed in their presentations.

Lastly, regarding the third argument, the Examiner again points to the "comprising" language employed in Applicants' rejected claims and maintains that such language does not preclude components which are not claimed. Thus, despite the fact that the composition "does not require" such components as Cremophor, said component is not precluded from the composition. Furthermore, regarding Applicants' remarks concerning the invention not comprising or utilizing Cremophor or any other solubilizing agent, the Examiner respectfully

directs Applicants to the instant claim 11, which expressly recites such compounds as Cremophor. Regarding Applicants' remarks that said component is or leads to cytotoxic conditions, it is also further pointed out that Applicants expressly discuss Cremophor as being an additive which may improve the solubility of paclitaxel and other insoluble drugs to achieve synergistic effect (pg. 7, lines 12-16).

Regarding each of the journal articles submitted by Applicants, though neither article is officially made of record, the Examiner has considered both for what they would have conveyed to the ordinarily skilled artisan at the time of the invention. Neither reference provides any compelling evidence which to support Applicants' assertions such that the obviousness rejections would be reconsidered and withdrawn.

For these reasons, Applicants' arguments are found unpersuasive. Said rejection is therefore **maintained** and extended to claims 75-78. Regarding claims 75 and 76, the previous rejection to claim 72 addresses the presence of the instantly claimed emulsifier. Gao further teaches that a typical composition of the practiced invention will comprise between about 10% to about 50% by weight of the composition of a surfactant (col. 8, line 54 to col. 9, line 3). Furthermore, surfactants are taught as referring to non-ionic surfactants and include such compounds as the instantly claimed Cremophor (claim 11) as well as the instantly claimed polysorbates or "Tween" compounds (e.g. Tween-20, -40, -60 and -80) (see col. 8, lines 25-45).

NEW REJECTIONS

In light of Applicants' newly added limitations (e.g. claim 78) as well as the claims which were not previously rejected, the following rejection has been newly added:

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 77 contains the trademarks/trade names "Brij", "Pluronic" and "Span". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, for example, the trademark/trade name "Pluronic" is used to identify/describe poloxamer or polyoxyethylene-polyoxypropylene copolymer compounds and, accordingly, the identification/description is indefinite.

All claims under consideration remain rejected; no claims are allowed.

CONCLUSION

Due to the new grounds of rejection, namely to claims 75-77 the merits of which were

previously overlooked by the Examiner, as discussed above, this action is deemed **non-final**.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615